CHEST

Lung Ultrasound in the ED

Will Death Do Us Part?

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Lung ultrasound (LUS) has become an important test for emergency point-of-care imaging.[1,2] Despite its growing adoption, LUS has failed to demonstrate improvements in mortality. But is it reasonable to expect LUS to reduce mortality? For the LUS enthusiasts, its high diagnostic accuracy alone is enough to justify adoption. For the LUS skeptics, cries of dissent will continue until definitive randomized controlled trials are performed. So what is a reasonable burden of proof before a point-of-care imaging test like LUS becomes standard practice? To answer this, let us first consider the current evidentiary landscape of LUS in the ED.

Ovesen et al[3] detail the LUS landscape in their study published in this issue of *CHEST*. They reviewed the study design, methodology, outcomes, and evidentiary trends of LUS in the ED. They identified the Fryback and Thornbury (F&T) levels of test effectiveness for each studies' primary outcome: level 1, technical efficacy; level 2, diagnostic accuracy efficacy; level 3, diagnostic thinking efficacy; level 4, therapeutic efficacy; level 5, patient outcome efficacy; and level 6, societal efficacy.[4] Additionally, they reported the indications, use, and study design. The authors sought particularly to focus on studies targeting F&T levels 3 through 6.

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Of the 406 LUS studies included, most were observational (375 studies [92%]), with only 18 studies (4%) being randomized controlled trials. Most studies (320 studies [79%]) were of diagnostic accuracy (F&T level 2) as the primary outcome, with only 50 studies using an F&T level of 3 through 6 (12%) as the primary outcome. Only two studies (0.5%) reported mortality as a primary outcome. The authors did not identify significant changes over time with respect to study design, outcomes, or F&T levels.

Is the relative abundance of observational and diagnostic accuracy studies unexpected? No. It reflects the relative nascence of LUS compared with other imaging methods. Observational and diagnostic accuracy studies represent earlier phases of diagnostic research arcs. Early phase 1 and 2 diagnostic accuracy studies ask whether LUS can differentiate healthy people from those harboring disease (and at what threshold).[5] Phase 3 diagnostic accuracy studies, that is, traditional diagnostic cohort studies, ask whether LUS can diagnose a condition in a patient who is at risk of the disease. For example, what is the accuracy of LUS to diagnose heart failure in patients seeking treatment at the ED with acute undifferentiated dyspnea? Phase 4 studies are the definitive diagnostic studies that attempt to address the higher F&T levels and whether integration of LUS into diagnostic pathways improves patient or health system outcomes.[5]

So, when do we need phase 4 (controlled trials) diagnostic studies and when is demonstrating excellent diagnostic accuracy enough? Like most things in research, it depends. If LUS has excellent diagnostic accuracy, the chance of missing an alternate diagnosis is low, and if an evidence-based intervention can be performed based on the findings, demonstrating excellent diagnostic accuracy may be enough to justify adoption.[5] Alternatively, and in many cases, LUS is not a definitive test, but rather is used to augment existing diagnostic pathways. In these cases, phase 4 studies demonstrating an additional diagnostic or therapeutic yield resulting from integration of LUS are important. These studies help to detect second-order effects resulting from integrating LUS, including the potential risk for premature diagnostic closure, failure to detect alternative diagnoses that would have been seen on a method like chest radiography, or time costs resulting

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from physicians performing the test at the bedside. So why is it that demonstrating a mortality benefit from LUS is so challenging? The problem lies not with LUS, but rather with how the test interplays with therapeutic management in acute care medicine.

In the sickest patients in whom earlier time to diagnosis conceivably would have the greatest impact on mortality, treatment is concurrent with the diagnostic workup. Think of a patient with severe undifferentiated respiratory failure: they may receive noninvasive ventilation, antibiotics, diuresis, and steroids empirically as diagnostic tests are performed. Unless LUS identifies an unexpected cause of respiratory failure (which is rare), regardless of whether LUS is performed, mortality is unchanged because the therapy already has been administered. This does not mean that LUS is not valuable in these patients. On the contrary, LUS can provide diagnostic certainty, can identify rare causes of respiratory failure upfront (eg, occult pneumothorax), can improve patient flow through the ED, and can prevent more expensive downstream tests. Of note, LUS still may offer significant improvements in patient outcomes in settings where traditional imaging methods are not available: rural, remote, austere, or military settings and those reached before hospital arrival. However, ongoing research in these areas is needed.

For less sick patients in whom traditional imaging may be delayed, LUS is more likely to improve time to diagnosis and time to appropriate therapy (eg, LUS enables pneumonia diagnosis at first physician contact, prompting treatment hours before chest radiography is performed). In these patients, given the low baseline mortality and less time-sensitive diagnoses at play, reducing time to treatment is unlikely to improve mortality.

So will LUS ever show a mortality reduction in a clinical trial? Maybe. One of the unique and often overlooked aspects of LUS (and point-of-care ultrasounds more broadly) is its ability to phenotype patients quickly into previously inaccessible groups that are defined from a combination of clinical history, anatomic information, and physiologic data that is uniquely available by ultrasound.[6-8] For example, LUS integrated with point-of-care echocardiography to assess for ejection fraction, velocity time integral, valvopathy, and left atrial filling pressures can help to differentiate causes of interstitial syndromes and to suggest therapies depending on the subtype of pulmonary congestion that is present (eg, inotropes vs decongestion). Hypoxia with consolidation consistent with lobar collapse on LUS (which is missed on chest radiography because of its lack of sensitivity) may benefit from early and aggressive chest physiotherapy, cough assist, or recruitment strategies. The key for these patients is that each diagnostic finding is accompanied by a therapy that currently is difficult or unable to be used in current diagnostic schemas.

So what is the future of LUS in the ED? Its accuracy and portability position it perfectly to sit at the center of a new era of phenotyped resuscitation, where previously unused or underused therapies are implemented based on multiorgan anatomic, physiologic, and pathologic data. With this strategy, one day, LUS might even demonstrate a reduction in mortality.

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None declared.

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